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09/926,002	10/30/2001	Ulf Schroder	SCHR300/ REF	6626

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EXAMINER
FORD, VANESSA L

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/926,002	Applicant(s) SCHRODER ET AL.	
	Examiner Vanessa L. Ford	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 1-10 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1-10 of copending Application No.09/926,601. Application No. 09/926,601 and 09/926,602 both teach antigens and adjuvants (i.e. monoglycerides comprising mono-olein and oleic acid). Application No. 09/926,602 discloses an antigen coupled to an immunogenically active carrier and adjuvant (i.e. monoglycerides comprising mono-olein and oleic acid). Svenson, *(WO 97/35616, published October 1997),* teaches the combination of antigen conjugated to immunogenically active carriers (IACs). Application No. 09/926,601 <u>does not</u> disclose immunogenically active carrier that are covalently bonded to the antigens. It would be obvious to prepare a vaccine with an antigen and adjuvant as set forth in Application No. 09/926,601 and to combine the antigen with the immunogenically active carrier as taught in Application No. 09/926,6002 as set forth by Svenson. The

disclosure of Svenson renders the invention of Application Nos. 09/926,601 overlapping with the invention set forth in Application No. 09/926,602 overlapping such that the claims in each are properly rejected under the judicially created doctrine of obviousness-type double patenting.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 1 is rejected under 35 U.S.C. 112, second pâragraph, as being indefinite.

Claim 1 is indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites the limitation "may". It is unclear as to if the acyl chain of the claimed invention contains one or more unsaturated bonds"? Does the acyl chain contain unsaturated bonds? How many unsaturated bonds are contained in the claimed invention? The metes and bonds of the claimed invention cannot be ascertained. Clarification is required.

3. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

Claim 3 is indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites the limitation "optionally". It is unclear as to how any unsaturated bonds are contained in the claimed

invention. The metes and bonds of the claimed invention cannot be ascertained. Clarification is required.

4. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

Claim 4 (line 3) recite "and" which renders the claim indefinite by reciting improper Markush language. Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being "selected from the group consisting of A, B and C." See Ex parte Markush, 1925 C.d. 126 (Comm'r Pat. 1925). It is unclear to which combinations of chemicals the claim is referring?

5. Claim 5 is indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites the limitation "possibly soybean oil". It is unclear as to if the soybean oil is used in the vaccine formulation? If soybean is used in the claimed invention, what percentage of soybean oil maybe used in the claimed invention? Clarification is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-4 and 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schroder *(WO 97/47320, published December 1997)* in view of *Svenson, WO 97/35616, published October 1997).*

Claims 1-4 and 6-9 are drawn to a vaccine formulation comprising as adjuvant one or more substances selected from a) monoglyceride preparations having 80% monoglyceride content, b) fatty acids and c) an immunizing component consisting of active carbohydrate moieties (ACM) derived from *Mycobacterium tuberculosis* which are each covalently coupled, possibly via identical divalent bride groups to immunogenically active carrier (IAC).

Schroder teaches the use of monoglycerides as adjuvants. Schroder teaches that the parenteral or mucosal administration of a pharmaceutical formulation containing monoglycerides (i.e. mono-olein/oleic acid) improves the immune response against admixed antigens/vaccines (page 4, lines 16-25). Schroder teaches that a combination between a monoglyceride and a fatty acid can stimulate the immune system to produce antibodies and induce protective immunity (page 7, lines 6-9). Limitations such as "mucosal administration is being view as a limitation of intended use. However, it is well known in the art that lipid preparations that are used as adjuvants are not restricted to one mode of administration and can be used in many routes of administration including mucosal. Limitations such as packaging the vaccine as an aersol, spray or nose-drop package is being viewed as a limitation of design choice.

Schroder does not teach an immunizing component consisting of active carbohydrate moieties (ACM) derived from *Mycobacterium tuberculosis* which are each covalently coupled, possibly via identical divalent bride groups to immunogenically active carrier (IAC).

Svenson teaches the use of carbohydrate moieties (ACM) which are covalently coupled possibly via identical divalent bridge groups to immunologically active carriers (IAC). Svenson teaches that bacterial polysaccharides are classical examples of antigens are not T helper cell-dependent and mainly induce IgM class of antibodies. Svenson teaches that in immunologically immature small children, the elderly and immunosuppressed persons polysaccharides are known to be poor immunogens or not at all immunogenic. Svenson teach that polysaccharide antigens which are chemically conjugated to carriers comprising T cell epitopes are effective as vaccines. It is well known in the art that the use of adjuvants with antigens enhance the immunogenicity of the antigen.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the monoglyceride preparation as taught by Schroder to the vaccine composition comprising of consisting of active carbohydrate moieties (ACM) of Svenson because Schroder et al teach that a combination between a monoglyceride and a fatty acid can stimulate the immune system to produce antibodies and induce protective immunity (page 7, lines 6-9). It would have been expected barring evidence to the contrary, that the addition of monoglycerides to compositions consisting of carbohydrate moieties (ACM) would provide enhanced immunogenicity of

antigens and the use of monoglycerides in vaccines are stable, cheaper and easy to formulate.

7. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schroder in view of Svenson as combined *supra* as applied to claims 1-4 and 6-9 above and in further view of Vercellone et al *(Frontiers in Bioscience, 1998 Aug 6;3:e149-63).*

Claim 5 is drawn to a vaccine formulation wherein the adjuvant is a mixture of mono-olein and oleic acid and possibly soybean oil and the immunizing component is lipoarabinomannan-tetanus toxoid (LAM-TT).

Schroder and Svenson as combined *supra* do not teach lipoarabinomannan-tetanus toxoid (LAM-TT).

Verecllone et al teach lipoarabinomannan (LAM) derived from *Mycobacterium tuberculosis*. Verecllone et al teach that LAM has a wide spectrum of immunological properties which contribute to protective immunity. Verecllone et al teaches that stimulates double negative T cells which contributes to the protective immunity against tuberculosis. Verecllone et al teach that Lam has the ability to insert into membranes without the involvement of any receptor. Verecllone et al also teach that T lymphocytes are involved in host defense by killing infected cells (page 16). It is well known in the art that carriers such as tetanus toxoid can be chemically conjugate to antigens to improve their immunogenicity and are used as vaccines.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was to further modify the vaccine composition as combined *supra* according to the teaching of Verecllone et al because Verecllone et al teaches that lipoarabinomannan has the ability to insert into membranes without the involvement of

any receptor and that lipoarabinomannan stimulates double negative T cells which contributes to the protective immunity against tuberculosis (page 16). It would have been expected barring evidence to the contrary, that the addition of lipoarabinomannan would provide enhanced immunogenicity of antigens, and therefore provide protective immunity.

8. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schroder *(WO 97/47320, published December 1997)* in view of Vercellone et al *(Frontiers in Bioscience,1998 Aug 6;3:e149-63).*

Claim 10 is drawn to a method of vaccinating a mammal against Tuberculosis which comprises mucosal administration to the mammal of an protection-inducing amount of a tuberculosis vaccine composition.

Schroder teaches a method of vaccinating mice comprising a diphtheria antigen and a monoglyceride preparation (page 9, example 4). Schroder teaches that both IgG as well as protective antibody titers were at the same level as compared to the control groups which received a composition of diptheria toxoid and alum. Schroder also teaches that the high IgG titers always were accompanied by high neutralization titers indicating that the formulations do no destroy the antigenic sites that are important for protective immunity (page 9, Example 4).

Schroder does not teach an immunizing component consisting of active carbohydrate moieties (ACM) derived from *Mycobacterium tuberculosis* which are each covalently coupled, possibly via identical divalent bride groups to immunogenically active carrier (IAC).

Schroder does not teach lipoarabinomannan-tetanus toxoid (LAM-TT).

Verecllone et al teach lipoarabinomannan (LAM) derived from *Mycobacterium tuberculosis*. Verecllone et al teach that LAM has a wide spectrum of immunological properties which contribute to protective immunity. Verecllone et al teaches that stimulates double negative T cells which contributes to the protective immunity against tuberculosis. Verecllone et al teach that Lam has the ability to insert into membranes without the involvement of any receptor. Verecllone et al also teach that T lymphocytes are involved in host defense by killing infected cells (page 16). It is well known in the art that carriers such as tetanus toxoid can be chemically conjugate to antigens to improve their immunogenicity and are used as vaccines.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the lipoarabinomannan as taught by Verecllone et al to the vaccine composition used in the method of vaccinating a mammal as taught by Schroder because Schroder et al teach that the parenteral or mucosal administration of a pharmaceutical formulation containing monoglycerides (i.e. mono-olein/oleic acid) improves the immune response against admixed antigens/vaccines (page 4, lines 16-25). It would have been expected barring evidence to the contrary, that the addition of lipoarabinomannan would provide enhanced immunogenicity of antigens and provide for enhanced protective immunity against Tuberculosis.

Status of Claims

9. No claims are allowed.

Conclusion

10. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
February 5, 2002

JAMES O. WILSON
PRIMARY EXAMINER
GROUP 1600